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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,006	11/20/2003	Nobuaki Hori	ABXJT.1C1C1C1C2	9100

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EXAMINER	
TUNGATURTHI, PARITHOSH K	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
11/08/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
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Office Action Summary	Application No.	Applicant(s)	
	10/719,006	HORI ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The finality of the previous office action mailed on 06/12/2007 is withdrawn upon further consideration. Please see the office action as set forth below.

Rejections Withdrawn

2. The rejection of claims 24-38 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 5-8 of U.S. Patent No. 6,677,138 in view of Trill et al (Current Opinion in Biotechnology. 1995. 6:553-560; IDS – 06/22/2006) as evidenced by Orlandi et al (Proc. Natl. Acad. Sci. USA, 86:3833-3837, 1989). Further, claims 24-38 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-13 and 15-27 of U.S. Patent No. 6,420,140; over Claims 1-4 and 6-11 of U.S. Patent No. 6,207,418; over Claims 1-4 and 6-11 of U.S. Patent No. 5,916,771, all in view of Trill (Current Opinion in Biotechnology. 1995. 6:553-560; IDS – 06/22/2006) is withdrawn in view of filing of appropriate terminal disclaimers.

3. The provisional rejection of claims 24-38 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 50, 51, 56, 58-65, 67 and 69-74 of copending Application No. 10/155,839 in view of Trill (Current Opinion in Biotechnology. 1995. 6:553-560; IDS – 06/22/2006) is withdrawn in view of abandonment of the copending Application No. 10/155,839.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 24-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing a human antibody (a) introducing a first polynucleotide into a first mammalian myeloma cell, wherein the first polynucleotide comprises a first amplifiable marker and a sequence encoding a heavy chain polypeptide of a human antibody; (b) introducing a second polynucleotide into a second mammalian myeloma cell, wherein the second polynucleotide comprises a second amplifiable marker and a sequence encoding a light chain polypeptide of the said human antibody; (c) culturing each of said first and second mammalian myeloma cells separately; and (d) fusing the cultured cells produced by steps (a)-(c) to form a hybrid cell, wherein the hybrid cell expresses the said human antibody, does not reasonably provide enablement for producing, does not reasonably provide enablement for (a) introducing a first polynucleotide ... (b) introducing a second ... (c) culturing each of said first and second mammalian myeloma cells separately in the presence of an amplification agent, wherein the first and second amplifiable markers are amplified by the same amplification agent; and (d) fusing the cultured cells produced by steps (a)-(c) to form a hybrid cell, wherein the hybrid cell expresses the said human antibody. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method for producing a human antibody, said method comprising: (a) introducing a first polynucleotide into a first mammalian myeloma cell, wherein the first polynucleotide comprises a first amplifiable marker and a sequence encoding a heavy chain polypeptide of a human antibody; (b) introducing a second polynucleotide into a second mammalian myeloma cell, wherein the second polynucleotide comprises a second amplifiable marker and a sequence encoding a light chain polypeptide of the said human antibody; (c) culturing each of said first and second mammalian myeloma cells separately in the presence of an amplification agent, wherein the first and second amplifiable markers are amplified by the same amplification agent; and (d) fusing the cultured cells produced by steps (a)-(c) to form a hybrid cell, wherein the hybrid cell expresses the said human antibody.

The specification teaches the generation of hybrid cells containing light and heavy immunoglobulin chains and states that the after the appropriate selection and

amplification, the selected first and second cells are fused to form the hybrid cell (example 1 in particular). However, the specification does not specifically disclose the amplification of the individual light and heavy chain genes. Particularly, in view of the art recognized problem, wherein the heavy chain expression alone is toxic to the cells, the specification fails to enable a skilled artisan to amplify the heavy chain in the absence of light chain.

MPEP 2161:
An invention may be described without the disclosure being enabling ... "[A] specification which describes' does not necessarily also enable' one skilled in the art to make or use the claimed invention." See In re Armbruster, 512 F.2d 676, 677, 185 USPQ 152, 153 (CCPA 1975).

The claims recite a method wherein the fusion of the two myeloma cells is carried out after the amplification of the heavy and light chains. However, due to the toxicity associated with the heavy chain production alone in cells and in the absence of the any working examples to overcome such art recognized deficiency, the specification does not enable a skilled artisan to amplify the heavy and light chain separately before fusion of myeloma cells. For example, Clive and Kaufman (U.S. Patent 6475787) teach that heavy chain expression in the absence of light chain expression may be deleterious to the producing cells (paragraph 6, in particular). Kohler (Proc. Natl. Acad. Sci. 1980, 77:2197-2199) teach that free immunoglobulin heavy chain is toxic for the cells (please see the entire article, abstract in particular). Haas and Wabl (Proc. Natl. Acad. Sci. 1984, 81:7185-7188) teach that immunoglobulin heavy chain toxicity. Haas and Wabl teach that it is very difficult to recover cells that have only H chain expression without any L chain expression (please see the entire article, introduction in particular).

Bebbington (Methods: A Companion to Methods of Enzymology, 1991. 2(2):136-145) teach that the synthesis of heavy chain without a light chain may be toxic to the cell and should be avoided (page 138 left column, in particular). All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in view of the art recognized problems, such as heavy chain toxicity.

The applicant has not overcome the art recognized deficiencies associated with amplification pre-fusion rather than the more common and accepted post-amplification protocol for optimal Ab expression.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, at the time the application was filed it would not have been predictable for one of skill in the art for the amplification of heavy chain in the absence of light chain as contemplated in the disclosure. Thus, it would require undue experimentation by one of skill in the art to practice the invention as claimed.

Conclusion

6. No claims are allowed

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi
Ph: (571) 272-8789

DAVID J. BLANCHARD
~~PATENT~~ EXAMINER
PRIMARY